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Development of In Vitro and In Vivo Model Systems for the Study of Lung Chemical Susceptibility and Carcinogenesis.

Section A: "In Vivo Model Systems Studies"

At the beginning of the new contract year on July 1, 1976 the following studies will be in progress and be carried over for completion:

- CTR 47: Subcutaneous Carcinogenic Bioassay of CSCF Material
- CTR 49: Intratracheal Carcinogenic Bioassay of CSCF Material
- CTR 50: Serial Sacrifice of BaP Intratracheal-Treated Mice for Definition of Histopathological Lesions
- CTR 51: Serial Sacrifice of MCA Intratracheal-Treated Mice for Definition of Histopathological Lesions

In an experimental series to be developed in 1976-79, primary emphasis will be to define the role of initiators, promoters and cocarcinogens. Such a model would be developed for the purpose of testing smoke and its constituents for their possible role in the carcinogenic process. Model experiments using known chemicals with known roles either as carcinogens, cocarcinogens, etc. would be performed to define this system; and tobacco smoke constituents would be integrated to test their effects in the systems developed.

Section B: "In Vivo and In Vitro Model Systems Studies"

The contractees propose to use a combination of in vivo - in vitro model systems to answer the following questions: Can tobacco-related products be analyzed for their tumor promoting effects in a cell culture system? Can these products be analyzed for their mutagenic, carcinogenic, or cytotoxic effects in an in vitro model system? Can these culture systems be made more sensitive, more discriminatory, and capable of determining the molecular mechanism for PAH-induced carcinogenesis, mutagenesis, and cytotoxicity?

The combination in vivo - in vitro model systems include two mutagenesis systems (one bacterial and one mammalian), and three cell transformation systems (BALB/3T3, 10 T 1/2 CL 8, and Syrian golden hamster fetal (SHE) cells). The biological effects to be examined, mutagenesis and cell transformation, can be quantitated in these model systems.

Activation Date: July 1, 1976

Current Contract Level: \$350,000.

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